

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year)
 31 May 2001 (31.05.01)

International application No.
 PCT/US99/16937

Applicant's or agent's file reference
 X-11634

International filing date (day/month/year)
 26 July 1999 (26.07.99)

Priority date (day/month/year)
 31 July 1998 (31.07.98)

Applicant

BAKER, Jeffrey, Clayton et al

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

02 December 1999 (02.12.99)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Dominique DELMAS

Telephone No.: (41-22) 338.83.38

BEST AVAILABLE COPY

SEARCH COPY

PCT
REQUEST

For receiving office use only

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

International Application No. (26.27.98)	PCT/US 99/16937
International Filing Date	26 JUL 1999
PCT INTERNATIONAL APPLICATION ROUS	
Name of Receiving Office and "PCT International Application"	
Applicant's or agent's file reference X-11634	

Box No. I TITLE OF INVENTION
CRYOGRANULATION OF ACTIVATED PROTEIN C
Box No. II APPLICANT

Name and address: *The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.*

ELI LILLY AND COMPANY
Lilly Corporate Center
Indianapolis, Indiana 46285
US

☐ This person is also inventor.

Telephone No.
(317) 276-7243

Facsimile No.
(317) 276-3861

Teleprinter No.
276051 ELI LILLY IND A

State (i.e. country) of nationality:
US

State (i.e. country) of residence:
US

This person is applicant for the purposes of:

☐ all designated States
 ☒ all designated States except the United States of America
 ☐ the United States of America only
 ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

Name and address:

BAKER, Jeffrey Clayton
114 East 44th Street
Indianapolis, Indiana 46205
US

This person is:

☐ applicant only
☒ applicant and inventor

☐ inventor only (If this check-box is marked, do not fill in below)

State (i.e. country) of nationality:
US

State (i.e. country) of residence:
US

This person is applicant for the purposes of:

☐ all designated States
 ☐ all designated States except the United States of America
 ☒ the United States of America only
 ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

☒ agent ☐ common representative

BARRETT, Brian P., CONRAD, Robert A., GAYLO, Paul J., HAMILTON, Amy E., HUNTER, Frederick D., KOIVUNIEMI, Paul J., SALES, James J.

Telephone No.
(317) 276-7243

ELI LILLY AND COMPANY
Lilly Corporate Center
Indianapolis, Indiana 46285
US

Facsimile No.
(317) 276-3861

Teleprinter No.
276051 ELI LILLY IND A

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Corresponds to: Form PCT/RO/101 (first sheet) (July 1998)

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS			
If none of the following sub-boxes is used, this sheet is not to be included in the request.			
Name and address: JONES, Nancy Delores 3149 Midvale Drive Indianapolis, Indiana 46222 US		This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below)	
State (i.e. country) of nationality: US		State (i.e. country) of residence: US	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box			
Name and address:		This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below)	
State (i.e. country) of nationality:		State (i.e. country) of residence:	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box			
Name and address:		This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below)	
State (i.e. country) of nationality:		State (i.e. country) of residence:	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box			
Name and address:		This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below)	
State (i.e. country) of nationality:		State (i.e. country) of residence:	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box			
Name and address:		This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below)	
State (i.e. country) of nationality:		State (i.e. country) of residence:	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box			

☐ Further applicants and/or (further) inventors are indicated on a continuation sheet

Corresponds to: Form PCT/RO/101 (continuation sheet) (July 1998)

Box No. V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

Regional Patent

- ☒ **AP** **ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA** **Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG, Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP** **European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA** **OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Cote d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on line)

National Patent (if other kind of protection or treatment desired, specify on line)

- | | |
|---|--|
| <input checked="" type="checkbox"/> AL Albania | <input checked="" type="checkbox"/> LS Lesotho |
| <input checked="" type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> LT Lithuania |
| <input checked="" type="checkbox"/> AT Austria | <input checked="" type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> LV Latvia |
| <input checked="" type="checkbox"/> AZ Azerbaijan | <input checked="" type="checkbox"/> MD Republic of Moldova |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina | <input checked="" type="checkbox"/> MG Madagascar |
| <input checked="" type="checkbox"/> BB Barbados | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BG Bulgaria | |
| <input checked="" type="checkbox"/> BR Brazil | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input checked="" type="checkbox"/> NO Norway |
| <input checked="" type="checkbox"/> CN China | <input checked="" type="checkbox"/> NZ New Zealand |
| <input checked="" type="checkbox"/> CU Cuba | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> DE Germany | <input checked="" type="checkbox"/> RO Romania |
| <input checked="" type="checkbox"/> DK Denmark | <input checked="" type="checkbox"/> RU Russian Federation |
| <input checked="" type="checkbox"/> EE Estonia | <input checked="" type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SE Sweden |
| <input checked="" type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> SG Singapore |
| <input checked="" type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> SI Slovenia |
| <input checked="" type="checkbox"/> GD Grenada | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> SL Sierra Leone |
| <input checked="" type="checkbox"/> GH Ghana | <input checked="" type="checkbox"/> TJ Tajikistan |
| <input checked="" type="checkbox"/> GM Gambia | <input checked="" type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> HR Croatia | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> ID Indonesia | <input checked="" type="checkbox"/> UA Ukraine |
| <input checked="" type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> IS Iceland | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> IN India | |
| <input checked="" type="checkbox"/> JP Japan | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> VN Viet Nam |
| | <input checked="" type="checkbox"/> YU Yugoslavia |
| <input checked="" type="checkbox"/> KG Kyrgyzstan | <input checked="" type="checkbox"/> ZW Zimbabwe |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet. |
| <input checked="" type="checkbox"/> KR Republic of Korea | |
| <input checked="" type="checkbox"/> KZ Kazakhstan | <input checked="" type="checkbox"/> AE United Arab Emirates |
| <input checked="" type="checkbox"/> LC Saint Lucia | <input checked="" type="checkbox"/> ZA South Africa |
| <input checked="" type="checkbox"/> LK Sri Lanka | |
| <input checked="" type="checkbox"/> LR Liberia | |

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

Corresponds to: Form PCT/RO/101 (second sheet) (January 1999)

Box No. VI PRIORITY CLAIM		Further priority claims are indicated in the Supplemental Box <input type="checkbox"/>		
		Where earlier application is:		
Filing date of earlier application (day/month/year)	Number of earlier application	National application: country	regional application:* regional Office	international application: receiving Office
item (1) 31 July 1998 (31.07.98)	60/094,969	US		
item (2)				
item (3)				
<input checked="" type="checkbox"/> The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s): (1)				
Box No. VII INTERNATIONAL SEARCHING AUTHORITY				
Choice of International Searching Authority (ISA) <i>(If two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):</i> ISA / US		Request to use results of earlier search; reference to that search <i>(if an earlier search has been carried out by or requested from the International Searching Authority)</i> Date) Number Country (day/month/year (or regional office)		
Box No. VIII CHECK LIST; LANGUAGE OF FILING				
This international application contains the following number of sheets: request : 04 description (excluding sequence listing part) : 12 claims : 01 abstract : 01 drawings : 00 sequence listing part of description : 00 Total number of sheets 18		This international application is accompanied by the item(s) marked below 1. <input checked="" type="checkbox"/> fee calculation sheet 2. <input checked="" type="checkbox"/> separate signed power of attorney (2) 3. <input checked="" type="checkbox"/> copy of general power of attorney and Delegation of Authority; reference number, if any: 4. <input type="checkbox"/> statement explaining lack of signature 5. <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s): 6. <input type="checkbox"/> translation of international application into (language): 7. <input type="checkbox"/> separate indications concerning deposited microorganisms or other biological material 8. <input type="checkbox"/> nucleotide and/or amino acid sequence listing in computer readable form 9. <input checked="" type="checkbox"/> other (specify) return receipt post card		
Figure of the drawings which should accompany the abstract		Language of filing of the international application: English		
Box No. IX SIGNATURE OF APPLICANT OR AGENT				
ELI LILLY AND COMPANY By: <u>Brian P. Barrett</u> Brian P. Barrett, Agent				

For receiving Office use only		2. Drawings: <input type="checkbox"/> received: <input type="checkbox"/> not received:
516 Rec'd PCT/PTO 26 JUL 1999 (26.07.99)		
ISA/US		
6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid		

Date of receipt of the record copy by the International Bureau:

For International Bureau use only

FEE CALCULATION SHEET

Annex to the Request

For receiving Office use only

PCT/US 99 / 1 6 9 3 7
International application No.Applicant's or agent's
file reference **X-11634**(26.07.99) 26 JUL 1999
Date stamp of the receiving OfficeApplicant
ELI LILLY AND COMPANY**Calculation of prescribed fees**

1. TRANSMITTAL FEE

\$240

T

\$ 240.00

2. SEARCH FEE

\$700

S

700.00

International search to be carried out by ISA/US

3. INTERNATIONAL FEE

Basic FeeThe international application contains 18 sheets
first 30 sheets

\$455

b₁

455.00

remaining 0 sheets X \$10 =

\$0

b₂

0

Add amounts entered at boxes b₁ and b₂
and enter total at B.

\$455

B

455.00

Designation FeeThe international application contains 79
designations.

\$1050

D

1050.00

10 designations X \$105=number of designation amount of
fees payable (maximum 11) designation fee

Add amounts entered at B and D and enter total at I.

\$1505

I

1505.00

4. FEE FOR PRIORITY DOCUMENT

\$15

P

15.00

5. TOTAL FEES PAYABLE

Add amounts entered at T, S, I and P.
and enter total in the TOTAL box.

USD \$2460

TOTAL

\$ 2460.00

☐ The designation fees are not paid at this time.**Mode of Payment**☒ authorization to charge deposit account ☐ cash☐ cheque☐ revenue stamps☐ postal money order☐ coupons☐ bank draft☐ other (specify):**Deposit Account Authorization**The RO/ US ☒ is hereby authorized to charge the total fees indicated above to my deposit account.☒ is hereby authorized to charge any deficiency or credit any overpayment in the
total fees indicated above to my deposit account☒ is hereby authorized to charge the fee for preparation and transmittal of the priority
document to the International Bureau of WIPO to my deposit account.

05-0840

26 July 1999
(26.07.99)

Brian P. Barrett

Deposit Account Number

Date (day/month/year)

Brian P. Barrett, Agent

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: BRIAN P. BARRETT
ELI LILLY AND COMPANY
LILLY CORPORATE CENTER
INDIANAPOLIS, IN 46285

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing
(day/month/year)

15 SEP 2000

Applicant's or agent's file reference

X-11634

IMPORTANT NOTIFICATION

International application No.

PCT/US99/16937

International filing date (day/month/year)

26 JULY 1999

Priority Date (day/month/year)

31 JULY 1998

Applicant

ELI LILLY AND COMPANY

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

CHRISTOPHER LOW

Donna Lawrence Fox

Telephone No. (703) 308-0196

PATENT COOPERATION TREATY


PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference X-11634	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/16937	International filing date (day/month/year) 26 JULY 1999	Priority date (day/month/year) 31 JULY 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant ELI LILLY AND COMPANY		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step or industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>

Date of submission of the demand 02 DECEMBER 1999	Date of completion of this report 22 AUGUST 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer  CHRISTOPHER LOW Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/16937

I. Basis of the report1. With regard to the **elements** of the international application:*☒ the international application as originally filed☒ the description:

pages 1-12 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the claims:

pages 13 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the drawings:

pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the sequence listing part of the description:

pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:☐ contained in the international application in printed form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☒ The amendments have resulted in the cancellation of:☒ the description, pages NONE☒ the claims, Nos. NONE☒ the drawings, sheets/fig NONE5. ☒ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/16937

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. statement**

Novelty (N)	Claims <u>1-8</u>	YES
	Claims <u>None</u>	NO
Inventive Step (IS)	Claims <u>None</u>	YES
	Claims <u>1-8</u>	NO
Industrial Applicability (IA)	Claims <u>1-8</u>	YES
	Claims <u>None</u>	NO

2. citations and explanations (Rule 70.7)

Claims 1-8 lack an inventive step under PCT Article 33(3) as being obvious over Tse et al. in view of Foster et al. Tse et al. teach similarly as the instantly claimed invention the use of a cryoprecipitate or cryogranulate procedure to prepare a stable fibrinogen composition from human origin which contains a high concentration of fibrinogen and very low levels of Factor VIII (FVIII). The dissolved cryoprecipitate is cooled to about 10° C to form cold-precipitate, then, the cold-precipitate is freeze-dried into cryogranules at -60° C or lower (i.e., frozen in liquid nitrogen).

Although, the reference does not specifically mention activated protein C, however, the reference clearly teaches the preparation of dissolved cryoprecipitate activated fibrinogen and FVIII. The activated fibrinogen and FVIII include the specific activated protein C since they are generic. For further support See e.g., the instant disclosure on page 1, lines 9-17 which acknowledges that protein C is a serine protease and naturally occurring anticoagulant that plays a role in the regulation of hemostasis by inactivating Factors Va and VIIIa in the coagulation cascade. Human protein C circulates as a 2-chain zymogen which is activated *in vivo* by thrombin and thrombomodulin on phospholipid surface resulting in activated protein C. Thus, in view of the above, the fibrinogen complex taught by the prior art clearly encompasses the instantly claimed activated protein C.

Tse et al. differ from claims 1-8 in not teaching a process of preparing a lyophilized formulation of activated protein C and the addition of a pharmaceutical acceptable bulking agent. With respect to lyophilization process, the reference of Tse et al. clearly teaches the use of lyophilized fibrinogen complex (See e.g., Figure 1 and col. 10, lines 1-4); however, the general method of lyophilization of protein pharmaceutical and the addition of a pharmaceutical bulking agent is conventional and within the ordinary skill in the art to which this invention pertains to lyophilize and add a pharmaceutically acceptable bulking agent of any protein of interest. Nevertheless, the lyophilization and the addition of a pharmaceutically acceptable bulking agent of activated protein C is clearly disclosed by (Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/16937

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): A61K 35/14, 38/00; C07K 17/00; C12P 21/06 and US Cl.: 530/384, 407, 411, 418; 435/68.1, 69.1; 514/2, 12

I. BASIS OF REPORT:

5. (Some) amendments are considered to go beyond the disclosure as filed:

NONE

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

Foster et al. on col. 9, lines 62 to col. 10, lines 5.

Thus, in view of the above, one of ordinary skill in the art would have been motivated to adapt the well known lyophilization process and addition of pharmaceutically acceptable bulking agent scheme of Foster et al. reference into the method of Tse et al. reference because including such features into the method of Tse et al. reference would have been obvious to one having ordinary skill in the art to obtain the known and recognized functions and advantages thereof. Therefore, the combined teachings of the prior art makes obvious a process of preparing cryogranules of activated protein C and a lyophilized formulation having a pharmaceutically acceptable bulking agent thereof.

Claims 1-8 meet the criteria as set forth by PCT Articles 33(2) and 33(4).

----- NEW CITATIONS -----

NONE